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[Claim(s)]

1.(a) Rapidly disintegrable compression molding characterized by containing excipient and (b) erythritol.

2. Rapidly disintegrable compression molding according to claim 1 which is one sort as which excipient is chosen from organic excipient which is one sort chosen from starch, celluloses, and sugar-alcohol, or two sorts or more, and inorganic excipient, or two sorts or more.

3. Rapidly disintegrable compression molding according to claim 2 whose starch is one sort chosen from corn starch, partial alpha-ized starch, and alpha-ized starch, or two sorts or more.

4. Rapidly disintegrable compression molding according to claim 3 whose starch is corn starch.

5. Rapidly disintegrable compression molding according to claim 2 whose celluloses are one sort chosen from crystalline cellulose, powdered cellulose, hydroxypropylcellulose, and carmellose, or two sorts or more.

6. Rapidly disintegrable compression molding according to claim 2 whose sugar-alcohol is one sort chosen from D-mannitol, xylitol, and maltitol, or two sorts or more.

7. Rapidly disintegrable compression molding according to claim 2 whose inorganic excipient is one sort chosen from synthetic hydrotalcite, precipitated calcium carbonate, and anhydrous dibasic calcium phosphate, or two sorts or more.

8. Claim 1 containing medicinal properties - rapidly disintegrable compression molding of seven given in any 1 clause.

Medicinal Properties 9. Vitamin Tablet, Alleviation-of-Fever Painkilling Antiphlogistic, Antihistamine, Antitussive, Rapidly disintegrable compression molding according to claim 8 which is one sort chosen from a fungicide, an antacid, a vegetable drug, a tunica-mucosa-ventriculi repairing agent, a painkilling spasmolytic, a constipation treating agent, H2 receptor

antagonist, an ulcer management agent, an antibiotic, a hypotensor, an antiarrhythmic, digestive medicine, the expectorant, an anti-vertigenous drug (motion sickness medicine), and central nervous system stimulants, or two sorts or more.

10. Rapidly disintegrable compression molding according to claim 8 whose medicinal properties are one sort chosen from cetraxate hydrochloride, cimetidine, famotidine, ranitidine hydrochloride, nizatidine, and roxatidine acetate hydrochloride, or two sorts or more.

11.(a) Claim 1 whose sum total loadings of an excipient and (b) erythritol are 30 to 99 weight % to the full weight of rapidly disintegrable compression molding - rapidly disintegrable compression molding of ten given in any 1 clause.

12.(b) Claim 1 whose loadings of the (a) excipient to erythritol are 5 to 100 weight % - rapidly disintegrable compression molding of 11 given in any 1 clause.

13. Claim 1 which is a tablet - rapidly disintegrable compression molding of 12 given in any 1 clause.

14. When Examining by the Procedure of Description in Clause of Tablet of Disintegration Test of Pharmacopoeia of Japan (with No Disk), The diameter or the maximum length of rapidly disintegrable compression molding the case below 8mm Less than 60 seconds, Claim 1 which is collapsed or dissolved [ case below 8mm or more 10mm / case below 10mm or more 15mm ] within in 240 seconds less than 180 seconds less than 120 seconds less than 90 seconds the case below 15mm or more 20mm in the case of 20mm or more - rapidly disintegrable compression molding of 13 given in any 1 clause.

15. When Contained in Oral Cavity, [ Diameter or the Maximum Length of Rapidly Disintegrable Compression Molding ] Less than 40 seconds the case below 8mm or more 10mm Less than 60 seconds, [ case below 8mm ] Claim 1 which is collapsed or dissolved [ case below 10mm or more 15mm ] within in 180 seconds less than 120 seconds less than 90 seconds the case below 15mm or more 20mm in the case of 20mm or more - rapidly disintegrable compression molding of 14 given in any 1 clause.

16. Claim 1 whose density of rapidly disintegrable compression molding is 800-1600mg/cm3 - rapidly disintegrable compression molding of 15 given in any 1 clause.

17. Hardness of Rapidly Disintegrable Compression Molding [ Diameter or the Maximum Length of Rapidly Disintegrable Compression Molding ] The case below 0.5kg or more and 8mm or more 10mm 1kg or more, [ case below 8mm ] Claim 1 which is what has [ case below 10mm or more 15mm ] 4kg or more the case below 2kg or more and 15mm or more 20mm in the case of 3kg or more and 20mm or more - rapidly disintegrable compression molding of 16 given in any 1 clause.

18.(a) The manufacturing method of the rapidly disintegrable compression molding characterized by the thing containing an excipient and (b) erythritol substantially done for compression molding of the constituent of a dry state.

19. The manufacturing method according to claim 18 whose compression molding is tableting.
20. The manufacturing method according to claim 18 or 19 whose pressure of compression molding is 400-2000kg/cm2.

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[Detailed Description of the Invention]
Rapidly disintegrable compression molding and its manufacturing method technical field This invention, In fields, such as a drug and food, when it has practically sufficient strength like the usual tablet on the handling of a tablet and being contained in inner mouth, or when it puts in into water, it is related with the rapidly disintegrable compression molding which has prompt disintegration and solubility, and its manufacturing method.
Background art Although a tablet, the capsule, the trochiscus, a chewable tablet, the pellet, the powder, etc. are known as dosage forms of the solid preparations for taking orally in the field of a drug and food, there are few dosage forms in consideration of the ease of carrying out of administration of a patient. Development of dosage forms which was suitable also for the old man, the child, or the patient also for whom a deglutition is difficult especially and which handling is easy and administration tends to carry out is desired. In a tablet or the capsule, water is needed at the time of administration, and when there are much large tablet and administration quantity, it is hard to understand, and there are problems, like it can use for the pharynx or an esophagus. In particular, by the old man, the child, or the patient for whom a deglutition is difficult, it may be large, and occasionally this problem is got blocked in a throat, and it may lapse into suffocation status or it may cause [ it adheres to an esophagus and ] inflammation under the influence of a medicine etc. Although it is the dosage forms which the trochiscus is gradually dissolved or collapsed by inner mouth, and are applied to the oral cavity, the pharynx, etc. and water is not needed, when it drinks by mistake, there is a possibility of getting it blocked in the pharynx or an esophagus. Although it is the dosage forms which crunch a chewable tablet and are taken and water is not needed, it is not suitable for the weak old man and weak child of biting strength taking. In the pellet and the powder, water is needed at the time of administration, and there is a problem which can remain in the oral cavity, or can steam at the time of administration, or enters between prostheses and causes a pain.
On the other hand in recent years, the intubation prescribing [ for the patient ]-a medicine method for inserting a stomach-tube catheter in taking orally or pernasality, and prescribing a medicine for the patient is enforced to the patient with an advanced disease for whom a deglutition is difficult. The present condition grinds a tablet and the pellet, or is made to carry out a suspension to 20-30ml of water, using the powder as it is, and the procedure of pouring

in into a stomach-tube catheter with a syringe is performed. However, there is a problem of operation being complicated and occasionally getting the inside diameter of a catheter blocked easily for a 2-4mm and thin reason.

From these backgrounds, as dosage forms suitable for an old man, a child or the patient for whom a deglutition is difficult, etc., when contained in inner mouth, or when it puts in into water, some dosage forms which collapse or dissolve promptly are known.

For example, to JP,S62-50445,B, after making the molding pocket of Pori chlorination plastic sheeting etc. fill up with, cool and freeze the solution which uses as the main ingredients gelatin containing a physic substance, the molding of the release matrix network structure object acquired by freeze-drying is indicated. Since this release matrix network structure object has the density of 10-200mg/ml, and collapses quickly in 1 to 5 seconds within the oral cavity and it is understood with saliva, it is indicated that it can prevent breathing out also in the patient who dislikes administration.

On the other hand, "Zydis (brand name)" of R.P.Scherer (Britain) is commercialized as a dissolution type tablet in the oral cavity in foreign countries. Although composition of this tablet is not clear, it is manufactured by lyophilization. However, there is a fault that it is so weak that the tablet manufactured by these lyophilization has weak strength and measurement of hardness is impossible for it although it has rapid disintegration. Moreover, the manufacturing facility of lyophilization is required, and since manufacture takes a long time, it is inferior to industrial production nature.

In the International-Publication number WO 93/No. 12769 gazette Carry out the suspension of a physic substance, milk sugar, and the mannitol to agar solution, fill up the molding pocket of a PTP (Press Through Package) sheet (product made from polypropylene) etc., and it is made to solidify in the shape of jelly. After carrying out reduced pressure drying, the disintegration tablet in the oral cavity which carries out the seal of the aluminum foil and is used as a press-through package article is indicated. This molding has the density of 400-1000mg/ml, and the decay time within the oral cavity is about 5 to 20 seconds. Moreover, it has the hardness of about 2kg, and is divided also in extraction from a press-through package, and it is indicated that there is no generating of collapse, a chip, etc. However, since strength is weak compared with the usual tablet, this molding is difficult to apply for types of packing other than press-through packages, such as bottle packing. Moreover, since manufacture takes a long time, industrial production nature is inferior.

Then, some disintegration tablets in the oral cavity manufactured by the tableting method are reported.

The dissolution type tablet in the oral cavity which tablets the mixture which contains in JP,H5-271054,A moisture which is the grade with which the particle surface of medicinal properties, a saccharide, and said saccharide becomes wet is indicated.

In the International-Publication number WO 93/No. 15724 gazette ** In making the excipient with a quick rate of dissolution to water into the subject of a tablet composition ingredient, and the process which tablets the tablet containing ** drug by wet granulation On the occasion of compression molding, the fast-melting lock characterized by two points of being [ it / what carries out compression molding before drying the kneaded object of the excipient and drug with a quick rate of dissolution to water ] ** is indicated.
A mold is filled up with the kneaded object which ** humidity carried out, and it is compressed into JP,H6-218028,A. The molding procedure of the tablet triturate which applied powder to the compression side or the compression punch surface of tablet triturate, and prevented with the tension at the time of compression of tablet triturate before compression molding of the molding procedure of the tablet triturate characterized by molding and ** tablet triturate is indicated.
In JP,H8-19589,A, the tablet manufacturing method which the hole for tablet molding is filled up, and at least one field of the humid powder in said hole sticks, and molds humid powder into the form of a tablet with a molding public-funds type through a prevention film is indicated.
It is a process by a wet tablet method, and since a wetting agent is contained at the time of molding and it is molded by low pressure, these procedures serve as a porous tablet which has moderate porosity after dryness, they are soft and excellent in disintegration.
However, in order to fill up with and compress bad fluid humid powder, there is a fault that restoration variation is large and easy to produce with tension. Moreover, the special drier dried with the form of soft molding maintained is required, and inferior to industrial production nature.
For this reason, the disintegration tablet in the oral cavity excellent in industrial production nature by the dry type tableting method is reported.
60g of relative bulk density / sorbitol particulate matter below 100ml is blended with the bad mannitol or the milk sugar of moldability with affinity low to JP,H5-310558,A, Loadings reduction of other additive agents with high moldability, for example, a cellulose system compound, an acrylic acid system compound, gelatin, etc. can be aimed at, and being obtained as a solid-preparations constituent excellent in disintegration is indicated.
The dissolution type compression molding in the oral cavity which has prompt disintegration and solubility in the oral cavity which contains the low saccharide of moldability and the high saccharide of moldability in the International-Publication number WO 95/No. 20380 gazette is indicated. This molding is a tablet with a diameter [ phi ] of 10mm, it has the hardness of 3-6kg, and the dissolution time within the oral cavity is indicated to be 15 to 25 seconds.
however -- if tableting preassure power is seen -- 50-400kg / pestle (64-509kg/cm2) -- it is a grade, and it becomes [ the tableting pressure of about 1000kg/cm2 of the usual tablet ], and is molded by low tableting preassure. From this, this molding is presumed to be what has weak

and quite weak dropping impact strength etc. compared with the usual tablet.
If disintegration and solubility will become quick if a tablet is generally molded by low tableting preassure, but hardness will become low and molds by high tableting preassure, the thing of high hardness will be obtained, but disintegration and solubility become late.
Although the conventional tablet has the strong hardness which does not collapse in a manufacturing process and a distribution process, by internal use, within an alimentary canal, it collapses and it dissolves, and since it aims at making medicinal properties emit, the prompt disintegration in the oral cavity and solubility are not taken into consideration.
Therefore, about the disintegration in the oral cavity, and solubility, it was not enough and there was no tablet which has prompt disintegration, solubility, and strong hardness simultaneously.
Therefore, when it puts in in the oral cavity and into water, while having prompt disintegration and solubility, it is necessary to develop the tablet which has the strong strength which does not collapse in a manufacturing process and a distribution process.
There is the purpose of this invention in offering the rapidly disintegrable compression molding which has the strong hardness which has prompt disintegration and solubility and does not collapse in a manufacturing process and a distribution process, when it puts in in the oral cavity and into water.
Other purposes of this invention are to offer the procedure which was excellent in the industrial production nature manufactured with the same dry method as the usual tableting method in the rapidly disintegrable compression molding which has the above outstanding characteristics without requiring a complicated process and special equipment.
Indication of invention Problem like the above If the mixture which contains the ingredient chosen from erythritol, an organic excipient, and an inorganic excipient as a result of inquiring wholeheartedly that it should solve is tableted When it had the strong hardness which does not collapse in a manufacturing process and a distribution process unexpectedly and put in in the oral cavity and into water, it found out that the rapidly disintegrable compression molding which has prompt disintegration and solubility was obtained, and this invention was completed.
That is, the rapidly disintegrable compression molding characterized by this invention containing the (a) excipient and (b) erythritol and its manufacturing method are offered.
Form of implementation of invention When rapidly disintegrable compression molding is compression molding which has practically sufficient strength in the manufacturing process and distribution process of a tablet and it contains in inner mouth in this invention, or when it puts in into water, it is the compression molding which has prompt disintegration and solubility.
As an excipient used for this invention, the organic excipient chosen from starch, celluloses, and sugar-alcohol and an inorganic excipient are mentioned.
Although corn starch, potatostarch, amylum tritici, rice starch, a partial alpha-ized starch, an

alpha-ized starch, hydroxypropyl starch, carboxy-methyl-starch sodium, etc. are mentioned as starch, Among these [ especially ], corn starch, a partial alpha-ized starch, and an alpha-ized starch are desirable. Although there is no restriction in particular about the particle size of the starch used for this invention, since it will be easy to produce a feeling of ZARATSUKI within the oral cavity if a particle size is large, a thing with a particle size of 500 micrometers or less is desirable.

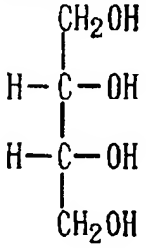
Although a crystalline cellulose, powdered cellulose, hydroxypropylcellulose, carmellose, carmellose calcium, crossing carmellose sodium, etc. are mentioned as celluloses, Among these [ especially ], a crystalline cellulose, powdered cellulose, hydroxypropylcellulose, and carmellose are desirable. Although there is no restriction in particular about the particle size of celluloses, since it will be easy to produce a feeling of ZARATSUKI within the oral cavity if a particle size is large, 500 micrometers or less are desirable.

Although it is sugar-alcohol other than erythritol, for example, D-mannitol, D-sorbitol, xylitol, maltitol, an anhydrous maltose, a water maltose, an anhydrous RAKUCHI torr, a water RAKUCHI torr, reduction malt sugar water American, etc. are mentioned as sugar-alcohol, Among these [ especially ], D-mannitol, xylitol, and maltitol are desirable. Although there is no restriction in particular about the particle size of the sugar-alcohol used for this invention, since it will be easy to produce a feeling of ZARATSUKI within the oral cavity if a particle size is large, a thing with a particle size of 500 micrometers or less is desirable.

As the inorganic excipient used for this invention Although **, synthetic hydrotalcite, precipitated calcium carbonate, anhydrous dibasic calcium phosphate, a water silicon dioxide, light anhydrous silicic acid, calcium silicate, magnesium aluminosilicate, magnesium oxide, magnesium hydroxide, etc. are mentioned Among these [ especially ], synthetic hydrotalcite, precipitated calcium carbonate, and anhydrous dibasic calcium phosphate are desirable. Although there is no restriction in particular about the particle size of an inorganic excipient, since it will be easy to produce a feeling of ZARATSUKI within the oral cavity if a particle size is large, the particle size of 500 micrometers or less is desirable.

Any one sort may be used for these excipients, and may be used for them combining two or more sorts.

The erythritol used for this invention is a grape sugar fermentation sweetener, and is sugar-alcohol of the tetravalence expressed with the following structural formula.



Erythritol is white crystalline powder of 119 degrees C of melting points, and is an edulcorant which melts into water easily, has a cold sense by heat-of-dissolution-42.9 cal/g, and there is no hygroscopicity and has 70 to 80% of degree of sweetness of sugar. Although there are no restrictions in particular in the particle size of the erythritol used for this invention, since it will be easy to produce a feeling of ZARATSUKI within the oral cavity if a particle size is large, a thing with a particle size of 500 micrometers or less is desirable.

(a) Although 30 to 99weight % of the range is suitable for the sum total loadings of an excipient and (b) erythritol to the full weight of rapidly disintegrable compression molding, they are 70 to 99 weight % still more preferably 50 to 99weight % more preferably. At less than 30 weight %, contribution of these ingredients falls and disintegration and solubility worsen.

Moreover, although 5 to 100weight % of the range is suitable for the loadings of the (a) excipient to (b) erythritol, they are 20 to 50 weight % still more preferably ten to 70weight % more preferably. (a) The tableting obstacle which originates in erythritol if an excipient is not blended (capping phenomenon: phenomenon in which the upper part of a tablet causes a horizontal crack in the shape of a hat)

Although it is easy to ******, if the (a) excipient is blended with (b) erythritol, such a tableting obstacle can be prevented. On the other hand, contribution of erythritol falls [ the loadings of the (a) excipient to (b) erythritol ] at 100 weight % or more, and decay and dissolution time become long. As for especially the case of celluloses, 5 to 50 weight % is desirable five to 70weight % to erythritol in particular.

As medicinal properties applied to this invention, there may not be any restriction in particular, it can add according to a use, and the thing of which form, such as powder, the shape of a crystal, oil, and solution form, may be used.

Moreover, you may add a taste ingredient instead of medicinal properties. It will be as follows if the example is given.

As a vitamin tablet, they are vitamin A, vitamin D, and vitamin E (acetic acid d-alpha-tocopherol etc.), for example, Vitamin B1 (thiamin hydrochloride etc.), vitamin B2 (riboflavin etc.), Vitamin B6 (pyridoxine hydrochloride etc.), vitamin C, vitamin B12 (ascorbic acid, sodium ascorbate, etc.) (acetic acid hydroxycobalamin etc.), a nicotinamide, calcium pantothenate, the pantethine, etc. are mentioned.

As an alleviation-of-fever painkilling antiphlogistic, aspirin, acetaminophen, ethenzamide, ibuprofen, ketoprofen, indomethacin, aminopyrine, etc. are mentioned, for example.

As an antihistamine, alimemazine tartrate, chlorpheniramine maleate, diphenhydramine hydrochloride, clemastine fumarate, the carbonoxamine maleate, dimenhydrinate, the meclizine hydrochloride, etc. are mentioned, for example.

As antitussive, codeine phosphate, dihydrocodeine phosphate, dextromethorphan hydrobromide, a noscapine, noscapine hydrochloride, etc. are mentioned, for example.

As a fungicide, cetylpyridinium chloride, dequalinium chloride, chlorhexidine hydrochloride, iodine, potassium iodide, etc. are mentioned, for example.
As an antacid **, magnesium aluminosilicate, magnesium aluminometasilicate, synthetic hydrotalcite, synthetic aluminum silicate, magnesium oxide, sodium bicarbonate, the magnesium carbonate, precipitated calcium carbonate, anhydrous dibasic calcium phosphate, scopolia extract, etc. are mentioned.
As a vegetable drug, the aloe, a fennel, a cork tree bark, a coptis root, a licorice, cinnamon, an amomi semen, a sialid, a rhubarb, a carrot, a malloti cortex, Corydalis tuber, a mahuang, etc. are mentioned, for example.
As a tunica-mucosa-ventriculi repairing agent, cetraxate hydrochloride, azulene sulfonate sodium, aldioxa, L-glutamine, sodium copper chlorophyllin, methyl methionine sulfonium chloride, etc. are mentioned, for example.
As a painkilling spasmolytic, N-methylscopolamine methylsulfuric acid salt, scopolamine hydrobromide, the methylatropine bromide, the scoplamine methylbromide, a belladonna extract, scopolia extract, ethyl aminobenzoate, a butylscopolamine bromide, a timepidium bromide, etc. are mentioned, for example.
As a constipation treating agent, the aloe, a rhubarb, bisacodyl, sodium picosulfate, etc. are mentioned, for example.
As a psychotropic drug, Timiperone, oxypertine, a diazepam, nitrazepam, flunitrazepam, lorazepam, haloperidol, prom peri DORU, etc. are mentioned, for example.
As an H2 receptor antagonist, cimetidine, famotidine, ranitidine hydrochloride, nizatidine, roxatidine acetate hydrochloride, etc. are mentioned, for example.
As an ulcer management agent, cetraxate hydrochloride, Teprenone, sulpiride, sucralfate, Plaunotol, gefalnate, etc. are mentioned, for example.
As an antibiotic, a tetracycline, oxytetracycline, methacycline, the doxycycline, the minocycline, chloramphenicols, and erythromycins are mentioned, for example.
As a hypotensor, BUTERARAJIN, hydralazine hydrochloride, etc. are mentioned, for example.
Pilsicainide hydrochloride, procainamide hydrochloride, etc. are mentioned as an antiarrhythmic.
As central nervous system stimulants, caffeine, anhydrous caffeine, caffeine and sodium benzoate, etc. are mentioned.
The medicinal properties used by this invention are used combining one sort or two sorts or more.
As desirable medicinal properties, a psychotropic drug, an antihistaminic, H2 receptor antagonist, an ulcer management agent, a vitamin tablet, digestive medicine, an antitussive and expectorant, a laxative, an anti-vertigenous drug (motion sickness medicine), central nervous system stimulants, etc. are mentioned. Moreover, not only the drug for human bodies

but an animal drug, agricultural chemicals, a diagnostic drug, etc. are mentioned. Moreover, you may apply to various uses which harnessed the characteristic of this invention, such as health food, a supplement, a ozostomia remover and a dental plaque stain, baths, and detergent.

Although the loadings of medicinal properties are based also on the character, they are 1 to 70 weight % usually [ of the whole formed element ] about 1 to 30 weight % still more preferably one to 50weight % preferably.

This invention may contain the various additive agents generally used for manufacture of a tablet, as long as there is no trouble in the effect of this invention.

As said additive agent, a lubricant, disintegrator, an excipient, a binder, colorant, an aromatizing agent, an edulcorant, corrigent, a foaming agent, a surface-active agent, etc. are mentioned, for example.

As a lubricant, the magnesium stearate, the calcium stearate, stearic acid, talc, sucrose fatty acid ester, a polyethylene glycol, hydrogenated oil, etc. are mentioned, for example.

As disintegrator, alginic acid, the calcium alginate, powdered tragacanth, crossing POPIDON, agar powder, a bentonite, etc. are mentioned, for example.

As an excipient, milk sugar, sucrose, grape sugar, fruit sugar, light anhydrous silicic acid, calcium silicate, a calcium lactate, etc. are mentioned.

As a binder **, gum arabic, sodium arginine, a carboxyvinyl polymer, Gelatin, a dextrin, pectin, sodium polyacrylate, a pullulan, a methylcellulose, hydroxypropylcellulose, the hydroxypropyl methylcellulose, a polyvinyl alcohol, a polyvinylpyrrolidone, a macro goal, etc. are mentioned.

As colorant, edible food color; edible rake pigments, such as Food Yellow No.5, Food Red No.2, and Food Blue No.2, yellow 32 iron oxide, 32 iron oxide, titanium oxide, beta-carotene, riboflavin, etc. are mentioned, for example.

As an aromatizing agent, Orange, Raimond, the peppermint, Mentor, various spice, etc. are mentioned, for example. As an edulcorant, saccharin sodium, Aspartame, glycyrrhizinate dipotassium, a stevia, thaumatin, etc. are mentioned, for example.

As corrigent, sodium chloride, the magnesium chloride, inosinic acid disodium, sodium L-glutamate monohydrate, honey, etc. are mentioned, for example.

As a foaming agent, the combination of acid, such as citric acid, tartaric acid, and a malic acid, and bases, such as sodium bicarbonate and sodium carbonate, is mentioned, for example.

As a surface-active agent, the polyoxyl 40 stearate, a sorbitan fatty acid ester, polyoxyethylene hydrogenated castor oil, polysorbate, the glyceryl monostearate, a sodium lauryl sulfate, etc. are mentioned, for example.

These additive agents may be added using one sort or two sorts or more at what kind of process of the manufacturing process of rapidly disintegrable compression molding. For example, it can add in proper quantity suitably at the process the time of granulation, or before

and behind them at the time of moisture addition at the time of mixture of medicinal properties, the (a) excipient, and (b) erythritol.

The rapidly disintegrable compression molding of this invention is a thing which contain the (a) excipient and (b) erythritol, for example and which is substantially done for compression molding of the constituent of a dry state, Medicinal properties and said additive agent are more specifically manufactured by tableting them as a dry state substantially after direct or granulation the (a) excipient, (b) erythritol, and if needed. It is as follows still in detail.

The 1st method Medicinal properties and said additive agent are mixed with the (a) excipient and (b) erythritol if needed, and compression molding is carried out (direct compression method).

the 2nd method grinding, after mixing medicinal properties and said additive agent with the (a) excipient and (b) erythritol if needed and carrying out compression molding at tabular compression molding or a slug lock (large-sized tablet) -- a request -- said additive agent -- in addition, compression molding is substantially carried out as a dry state (the dry granulation-tableting method).

The 3rd method Request after mixing medicinal properties and said additive agent with the (a) excipient and (b) erythritol if needed, adding and carrying out granulation of the solution or the suspension of water or starch, or/and sugar-alcohol and drying substantially Said additive agent is added and compression molding is substantially carried out as a dry state (the wet agglomeration-tableting method).

The 4th method Medicinal properties are divided into A group and B group, by the wet granulation of the 3rd method, after adjusting each granulation, said additive agent is added by request and compression molding is substantially carried out as a dry state (the multi-granulation-tableting method).

Manufacture of the rapidly disintegrable compression molding of this invention is performed by the equipment generally used by manufacture of the tablet. Specifically, as for mixture, a V shaped rotary mixer, a fluid bed granulation drier, an agitation granulation machine, a NAUTA mixer, a crossing rotary type mixer, etc. are used.

As for tabular compression molding of dry granulation, a dry granulation machine is used, and, as for compression molding of a slug lock, a rotary type tableting machine is used.

As for wet agglomeration, a fluid bed granulation drier, rolling fluidized-bed-granulation coating equipment, an agitation granulation machine, a cylinder pellet mill, a wet pellet mill, etc. are used.

The equipment with which compression molding is generally used for molding of a tablet is used, for example, single punch tableting, a rotary type tableting machine, a rotary type lamination tableting machine, etc. are mentioned.

What is necessary is just to set up arbitrarily the molding pressure power in the case of

tableting from the disintegration when putting in in the hardness of molding, and the oral cavity, and into water, and solubility. However, one of the features of this invention is that the disintegration when putting in in the oral cavity and into water and solubility are not greatly spoiled even if it heightens molding pressure power. Therefore, molding pressure power is comparable as the usual tablet, and is good, and 600-1800kg/cm2 400-2000kg/cm2 is about 800-1600kg/cm2 more preferably. the density of molding -- 800-1600mg/cm3 and the case where hardness is [ the diameter or the maximum length of rapidly disintegrable compression molding ] 10mm in about three 1000 - 1400 mg/cm preferably -- 2kg or more -- desirable -- 2-15kg -- more -- desirable -- 3-10kg What is necessary is just to set up to have.

The rapidly disintegrable compression molding of this invention obtained in this way is excellent in the disintegration when putting in in the oral cavity and into water, and solubility, and its hardness is high, and its dropping impact strength is also still stronger.

Although the disintegration of the rapidly disintegrable compression molding of this invention or solubility changes also with the sizes, [ the decay time (measured value by the disintegration test (with no disk) indicated in the clause of the tablet of the 12th amendment of the Pharmacopoeia of Japan) by the Pharmacopoeia of Japan ] As for the diameter or the maximum length of rapidly disintegrable compression molding, it is [ case below 8mm / case below less than 60 seconds and 8mm or more 10mm ] desirable [ case below less than 90 seconds and 10mm or more 15mm / case below less than 120 seconds and 15mm or more 20mm ] that it is less than 240 seconds in the case of less than 180 seconds and 20mm or more. Moreover, the disintegration within the oral cavity or solubility is a time of containing in the oral cavity. The diameter or the maximum length of rapidly disintegrable compression molding the case below 8mm Less than 40 seconds, What is collapsed or dissolved [ case below 8mm or more 10mm / case below 10mm or more 15mm ] within in 180 seconds less than 120 seconds less than 90 seconds less than 60 seconds the case below 15mm or more 20mm in the case of 20mm or more is desirable. the case where the diameter or the maximum length of rapidly disintegrable compression molding of the example of still more desirable disintegration is 10mm -- usually -- it is about 5 to 30 seconds still more preferably for 5 to 60 seconds preferably for 5 to 120 seconds. decay within the oral cavity, and dissolution time (time until moisture is not included in a mouth within a healthy adult man's oral cavity but a tablet dissolves completely only with saliva) -- usually -- it is about 5 to 30 seconds still more preferably for 5 to 60 seconds preferably for 5 to 90 seconds.

When contained in inner mouth, it collapses or dissolves gradually with saliva, but the rapidly disintegrable compression molding of this invention collapses or dissolves by the pressure by the pressure, i.e., upper AGO, and the tongue in the oral cavity or friction by a tongue, i.e., operation "to lick", more for a short time. In the person in the oral cavity who got dry, or a man with little saliva, even if it may use water or hot water, and you may collapse and dissolve

within the oral cavity or it takes as it is with water as well as the usual tablet, it does not interfere at all.
In addition, since it does not collapse and dissolve in an instant (for example, less than 1 second), the rapidly disintegrable compression molding of this invention can be included in inner mouth, can also taste mouthfeel, and if , it can also be breathed out.
On the other hand, 2-15kg of hardness (measured value by the tablet sclerometer) of the rapidly disintegrable compression molding of this invention is of 2kg or more usually about 3-10kg still more preferably preferably, when the diameter or the maximum length of rapidly disintegrable compression molding is 10mm. dropping impact strength (breakage rate: (breakage tablet / examination tablet) xwhen dropping tablet on stainless plate from height of 50cm 100 (%)) -- usually -- it is 0% more preferably about 0 to 20% about 0 to 50%.
Therefore, the rapidly disintegrable compression molding of this invention has the strong hardness which does not collapse in the manufacturing process and distribution process of a tablet, is equal also to extraction from a press-through package enough, and has hardness further applicable also to bottle packing (packing which put the tablet into containers, such as glass and plastics). Although the extraction hardness from the aluminum sheet of the usual press-through package changes with the size of a tablet, and form, in the case of 1kg or more and 10mm diameter, 2kg or more is [ case 8mm in diameter ] that is, desirable [ hardness ], for example. Moreover, as hardness of the tablet which can bear the shock of a distribution process by bottle packing, 3kg or more is desirable at a case 10mm in diameter.
On the other hand, since the rapidly disintegrable compression molding of this invention uses the erythritol of the edulcorant for the base, it has a cold sense and its taste is sweet. since [ moreover, ] erythritol is sugar-alcohol and Maillard reaction [browning phenomenon (it is also called amino-carbonyl reaction) by the reaction of amino acid and a saccharide] does not produce it like other sugar-alcohol, Even if it contains the medicinal properties which have an amino group, a browning phenomenon does not happen easily, and stability with the passage of time is good.
The rapidly disintegrable compression molding of this invention can be used for various sick treatment and prevention like the conventional tablet as the tablet which is easy to take also for an old man or a child, and a safe tablet for a general adult, and, moreover, is excellent in prolonged preservation and stability.
Although the form in particular of the rapidly disintegrable compression molding of this invention is not restricted, it can mention tablets, such as a triangle, a quadrangle, a round shape, form of an animal or a variant lock (Caplet type), a ring lock (the shape of a doughnut), a lamination lock, and dry coated tablets. Moreover, the mark for discernment, a character, etc. can be attached. Furthermore, you may be covered with the coating method generally used in manufacture of coated formulation.

. Although a work example is given to below and this invention is explained to it in more detail, these do not limit this invention.

Test method In order to explain the effect of this invention still in detail, it examined [ tablet / which was obtained in the example of reference, and the work example ] about the following tablet characteristics.

(1) Hardness test Tablet sclerometer [Freund Industrial, Inc.: The hardness of the diameter direction was measured using SHUROINIGERU tablet sclerometer]. An examination is done about 5 doses and the average value is shown.

(2) The decay in the oral cavity, extraction test Time until a tablet collapses and dissolves completely with the saliva (water is not included in a mouth) in the oral cavity of healthy adult-man trinominal (25 years old, 30 years old, 30 years old) was measured. A result shows the average value of trinominal.

(3) Disintegration test It measured according to the disintegration test indicated in the clause of the tablet of the 12th amendment of the Pharmacopoeia of Japan, without using a disk [a Toyama Industrial:disintegration test machine]. An examination is done about 6 doses and the average value is shown.

(4) Drop impact test The breakage rate when dropping a tablet on a stainless plate from a height of 50cm was measured. An examination is done about 10 doses and the breakage rate is shown.

(5) Tableting preassure power Tableting preassure power is measured and the value (kg/cm2) converted into the tableting preassure per pestle (kg/pestle) and the tableting preassure per unit area about the average tableting preassure is shown.

(6) Tablet density The weight of a tablet and thickness were measured about 10 doses, and it asked for tablet density from the following formula using the average value. Tablet density = example 1 of volume reference of the weight/tablet of a tablet After adding erythritol [Nikken Chemicals Co., Ltd. make:42-mesh (350 micrometers) path article] and milk sugar by the formula of the following table 1 of 1 to the agitation granulation machine, respectively and mixing for 3 minutes to it as an object for reference, 40ml of water was added and granulation was performed. It dried after granulation using the fluid bed granulation drier, and screening was carried out by 16 mesh sieves (1000 micrometers), and the magnesium stearate was added 0.5weight % and it mixed. Next, it tableted with the pestle of the 10mmphi round-corner planum using the single-engined tableting machine by the tablet weight of 400mg, and three kinds of tableting preassure power. The result examined about the obtained tablet is shown in 1 of the following table 2.

Example 2 of reference As an object for reference, the milk sugar of the example 1 of reference was replaced with anhydrous grape sugar, and the same operation as the example 1 of reference was performed by the formula of Table 1 of 2. The result examined about the

obtained tablet is shown in 2 of Table 2.

Example 3 of reference As an object for reference, the milk sugar of the example 1 of reference was replaced with sucrose, and the same operation as a comparative example 1 was performed by the formula of Table 1 of 3. The result examined about the obtained tablet is shown in 3 of Table 3.

Example 4 of reference As the object for reference In a fluid bed granulation drier, [ erythritol [Nikken Chemicals Co., Ltd. make:42 mesh (350 micrometers) path article] and milk sugar ] After adding by the formula of the following table 1 of 4, respectively and mixing for 3 minutes, 200ml of 5 w/v% solution of a polyvinyl alcohol is used, and they are the spray pressure of 2kg/cm2, and spraying liquid speed 20 ml/min. Granulation was performed.

Screening was carried out by 16 mesh sieves (1000 micrometers) after dryness, and the magnesium stearate was added 0.5weight % and it mixed. Next, it tableted with the pestle of the 10mmphi round-corner planum using the single-engined tableting machine by the tablet weight of 400mg, and three kinds of tableting preassure power. The result examined about the obtained tablet is shown in 4 of the following table 3.

表1　処　方

| 参　考　例 | | 1 | 2 | 3 | 4 |
|---|---|---|---|---|---|
| 成分 | エリスリトール | 350 g | 350 g | 350 g | 560 g |
| | 乳糖 | 150 g | − | − | 230 g |
| | 無水ブドウ糖 | − | 150 g | − | − |
| | 白糖 | − | − | 150 g | − |
| | ポリビニルアルコール | − | − | − | 10 g |
| 合　計 | | 500 g | 500 g | 500 g | 800 g |

表2　製剤特性

| 参考例 | | 1 | | | 2 | | |
|---|---|---|---|---|---|---|---|
| 打錠圧 | (kg／杵) | 598 | 722 | 1063 | 452 | 636 | 1126 |
| | (kg／cm²) | 762 | 920 | 1354 | 576 | 810 | 1434 |
| 硬度 | (kg) | 1.4 | 1.8 | 2.1 | 0.9 | 1.3 | 2.5 |
| 口腔内崩壊、溶解時間（秒） | | 37 | 43 | 45 | 46 | 58 | 77 |
| 崩壊時間（秒） | | 46 | 39 | 30 | 43 | 50 | 65 |
| 落下衝撃強度（%） | | 30 | 10 | 30 | 10 | 30 | 30 |
| 密度（mg／cm³） | | 1193 | 1210 | 1240 | 1156 | 1207 | 1251 |
| 備考 | | 硬度上がらず、1000kg／cm²以上でキャッピング発生 | | | 硬度上がらず、1000kg／cm²以上でキャッピング発生 | | |

表3　製剤特性

| 参考例 | | 3 | | | 4 | | |
|---|---|---|---|---|---|---|---|
| 打錠圧 | (kg／杵) | 467 | 690 | 995 | 695 | 1033 | 1247 |
| | (kg／cm²) | 595 | 879 | 1268 | 885 | 1316 | 1588 |
| 硬度 | (kg) | 1.3 | 2.0 | 2.7 | 2.0 | 3.9 | 4.9 |
| 口腔内崩壊、溶解時間（秒） | | 95 | 124 | 150 | 174 | 239 | 261 |
| 崩壊時間（秒） | | 12 | 12 | 14 | 93 | 112 | 146 |
| 落下衝撃強度（%） | | 10 | 20 | 30 | 10 | 0 | 0 |
| 密度（mg／cm³） | | 1174 | 1214 | 1243 | 1205 | 1241 | 1252 |
| 備考 | | 硬度上がらず、1000kg／cm²以上でキャッピング発生 | | | 口腔内崩壊時間が長い。<br>キャッピングはなし | | |

Work example 1 To a fluid bed granulation drier, they are erythritol [Nikken Chemicals Co., Ltd. make:42-mesh (350 micrometers) path article] and corn starch. After adding by the formula of the following table 4 of 1, respectively and mixing for 3 minutes, 800ml of water is used, and they are the spray pressure of 2kg/cm2, and spraying liquid speed 20 ml/min. Granulation was performed. Screening was carried out by 16 mesh sieves (1000 micrometers) after dryness, and the magnesium stearate was added 0.5weight % and it mixed. Next, it tableted with the

pestle of the 10mmphi round-corner planum using the single-engined tableting machine by the tablet weight of 400mg, and three kinds of tableting preassure power. The result examined about the obtained tablet is shown in 1 of the following table 5.
Work example 2 The corn starch of the work example 1 was replaced with the crystalline cellulose, and the same operation as a work example 1 was performed by the formula of Table 4 of 2. The result examined about the obtained tablet is shown in 2 of Table 5.
Work example 3 The corn starch of the work example 1 was replaced with corn starch and a partial alpha-ized starch, and the same operation as a work example 1 was performed by the formula of Table 4 of 3. The result examined about the obtained tablet is shown in 3 of Table 6.

Work example 4 The corn starch of the work example 1 was replaced with corn starch, the crystalline cellulose, and the partial alpha-ized starch, and the same operation as a work example 1 was performed by the formula of Table 4 of 4. The result examined about the obtained tablet is shown in 4 of Table 6.

表4　処　方

| 実　施　例 | | 1 | 2 | 3 | 4 |
|---|---|---|---|---|---|
| 成分 | エリスリトール | 560g | 560g | 560g | 560g |
| | トウモロコシデンプン | 240g | − | 120g | 120g |
| | 結晶セルロース | − | 240g | − | 40g |
| | 部分アルファー化デンプン | − | − | 120g | 80g |
| 合　計 | | 800g | 800g | 800g | 800g |

表5　製剤特性

| 実　施　例 | | 1 | | | 2 | | |
|---|---|---|---|---|---|---|---|
| 打錠圧 | (kg／杵) | 722 | 1091 | 1275 | 531 | 696 | 1021 |
| | (kg／cm²) | 920 | 1390 | 1624 | 676 | 887 | 1301 |
| 硬度 | (kg) | 1.9 | 4.0 | 4.9 | 3.6 | 5.0 | 7.3 |
| 口腔内崩壊、溶解時間（秒） | | 12 | 16 | 22 | 12 | 17 | 22 |
| 崩壊時間（秒） | | 15 | 20 | 24 | 10 | 11 | 14 |
| 落下衝撃強度（%） | | 0 | 0 | 0 | 0 | 0 | 0 |
| 密度（mg／cm³） | | 1162 | 1227 | 1246 | 1121 | 1164 | 1222 |
| 備　考 | | キャッピングなし<br>ザラツキ感なし | | | キャッピングなし<br>ザラツキ感なし | | |

表6　製剤特性

| 実　施　例 | | 3 | | | 4 | | |
|---|---|---|---|---|---|---|---|
| 打錠圧 | (kg／杵) | 706 | 1063 | 1176 | 729 | 1016 | 1224 |
| | (kg／cm²) | 899 | 1354 | 1498 | 929 | 1294 | 1559 |
| 硬度 | (kg) | 1.9 | 3.9 | 4.6 | 1.2 | 2.1 | 3.0 |
| 口腔内崩壊、溶解時間（秒） | | 13 | 16 | 16 | 18 | 24 | 28 |
| 崩壊時間（秒） | | 31 | 34 | 35 | 35 | 43 | 37 |
| 落下衝撃強度（%） | | 20 | 0 | 0 | 0 | 0 | 0 |
| 密度（mg／cm³） | | 1137 | 1195 | 1211 | 1115 | 1164 | 1190 |
| 備　考 | | キャッピングなし<br>ザラツキ感なし | | | キャッピングなし<br>ザラツキ感なし | | |

Work example 5 To a fluid bed granulation drier, they are erythritol [Nikken Chemicals Co., Ltd. make:42-mesh (350 micrometers) path article] and corn starch. After adding by the formula of the following table 7 of 5, respectively and mixing for 3 minutes, 175ml of 20 w/v% solution of D-mannitol is used, and they are the spray pressure of 2kg/cm2, and spraying liquid speed 18 ml/min. Granulation was performed.

Screening was carried out by 16 mesh sieves (1000 micrometers) after dryness, and the

magnesium stearate was added 0.5weight % and it mixed. Next, it tableted with the pestle of the 10mmphi round-corner planum using the single-engined tableting machine by the tablet weight of 400mg, and three kinds of tableting preassure power. The result examined about the obtained tablet is shown in 5 of the following table 8.
Work example 6 The corn starch of the work example 5 was replaced with corn starch and a crystalline cellulose, and the same operation as a work example 5 was performed by the formula of Table 7 of 6. The result examined about the obtained tablet is shown in 6 of Table 8.

表7　処方

| 実施例 | | 5 | 6 |
|---|---|---|---|
| 成分 | エリスリトール | 560g | 560g |
| | トウモロコシデンプン | 205g | 45g |
| | 結晶セルロース | − | 160g |
| | D−マンニトール | 35g | 35g |
| 合計 | | 800g | 800g |

表8　製剤特性

| 実施例 | | 5 | | | 6 | | |
|---|---|---|---|---|---|---|---|
| 打錠圧 | (kg/杵) | 826 | 1037 | 1446 | 552 | 703 | 920 |
| | (kg/cm$^2$) | 1052 | 1321 | 1842 | 703 | 895 | 1172 |
| 硬度 | (kg) | 0.9 | 1.5 | 3.0 | 3.1 | 4.3 | 5.9 |
| 口腔内崩壊、溶解時間(秒) | | 19 | 23 | 29 | 23 | 27 | 33 |
| 崩壊時間(秒) | | 24 | 27 | 28 | 26 | 26 | 26 |
| 落下衝撃強度(%) | | 20 | 10 | 0 | 0 | 0 | 0 |
| 密度(mg/cm$^3$) | | 1135 | 1169 | 1218 | 1128 | 1168 | 1205 |
| 備考 | | キャッピングなし ザラツキ感なし | | | キャッピングなし ザラツキ感なし | | |

Work example 7 To a fluid bed granulation drier, they are erythritol [Nikken Chemicals Co., Ltd. make:42-mesh (350 micrometers) path article] and corn starch. After adding by the formula of the following table 9 of 7, respectively and mixing for 3 minutes, 32ml of 70 w/v% solution of

xylitol is used, and they are the spray pressure of 2kg/cm2, and spraying liquid speed 6 ml/min. Granulation was performed. Screening was carried out by 16 mesh sieves (1000 micrometers) after dryness, and the magnesium stearate was added 0.5weight % and it mixed. Next, it tableted with the pestle of the 10mmphi round-corner planum using the single-engined tableting machine by the tablet weight of 400mg, and three kinds of tableting preassure power. The result examined about the obtained tablet is shown in 7 of the following table 10.

Work example 8 After having replaced the corn starch of the work example 7 with corn starch and a crystalline cellulose, adding by the formula of Table 9 of 8 and mixing for 3 minutes, the same operation as a work example 7 was performed using 200ml of 8 w/v% solution of xylitol. The result examined about the obtained tablet is shown in 8 of Table 10.

表9　処方

| 実施例 | | 7 | 8 |
|---|---|---|---|
| 成分 | エリスリトール | 560g | 560g |
| | トウモロコシデンプン | 217.6g | 64g |
| | 結晶セルロース | − | 160g |
| | キシリトール | 22.4g | 16g |
| 合計 | | 800g | 800g |

表10　製剤特性

| 実施例 | | 7 | | | 8 | | |
|---|---|---|---|---|---|---|---|
| 打錠圧 | (kg/杵) | 836 | 1009 | 1259 | 481 | 713 | 837 |
| | (kg/cm²) | 1065 | 1285 | 1604 | 613 | 908 | 1066 |
| 硬度 (kg) | | 1.1 | 1.4 | 2.2 | 2.9 | 5.3 | 6.3 |
| 口腔内崩壊、溶解時間(秒) | | 20 | 22 | 26 | 15 | 23 | 31 |
| 崩壊時間(秒) | | 63 | 57 | 65 | 23 | 25 | 30 |
| 落下衝撃強度(%) | | 10 | 10 | 0 | 0 | 0 | 0 |
| 密度(mg/cm³) | | 1139 | 1165 | 1191 | 1109 | 1171 | 1195 |
| 備考 | | キャッピングなし ザラツキ感なし | | | キャッピングなし ザラツキ感なし | | |

Work example 9 To a fluid bed granulation drier, they are erythritol [Nikken Chemicals Co., Ltd.

make:42-mesh (350 micrometers) path article] and synthetic hydrotalcite. After adding by the formula of the following table 11 of 9, respectively and mixing for 3 minutes, 800ml of water is used, and they are the spray pressure of 2kg/cm2, and spraying liquid speed 20 ml/min. Granulation was performed. Screening was carried out by 16 mesh sieves (1000 micrometers) after dryness, and the magnesium stearate was added 0.5weight % and it mixed.
Next, it tableted with the pestle of the 10mmphi round-corner planum using the single-engined tableting machine by the tablet weight of 400mg, and three kinds of tableting preassure power. The result examined about the obtained tablet is shown in 9 of the following table 12.
Work example 10 The synthetic hydrotalcite of the work example 9 was replaced with precipitated calcium carbonate, and the same operation as a work example 9 was performed by the formula of Table 11 of 10. The result examined about the obtained tablet is shown in 10 of Table 12.

表１１　処　方

| 実　施　例 | | 9 | 10 |
|---|---|---|---|
| 成分 | エリスリトール | 560ｇ | 560ｇ |
| | 合成ヒドロタルサイト | 240ｇ | － |
| | 沈降炭酸カルシウム | － | 240ｇ |
| 合　　計 | | 800ｇ | 800ｇ |

表１２　製剤特性

| 実　施　例 | | 9 | | | 10 | |
|---|---|---|---|---|---|---|
| 打錠圧 | (kg／杵) | 696 | 833 | 1245 | 760 | 945 |
| | (kg／cm²) | 887 | 1062 | 1586 | 968 | 1204 |
| 硬度 (kg) | | 2.1 | 2.8 | 5.5 | 2.1 | 2.7 |
| 口腔内崩壊、溶解時間（秒） | | 13 | 14 | 19 | 42 | 47 |
| 崩壊時間（秒） | | 19 | 21 | 21 | 106 | 100 |
| 落下衝撃強度（%） | | 0 | 0 | 0 | 20 | 10 |
| 密度（mg／cm³） | | 1106 | 1132 | 1197 | 1301 | 1326 |
| 備　考 | | キャッピングなし ザラツキ感なし | | | キャッピングなし ザラツキ感なし | |

Work example 11 To a fluid bed granulation drier, they are erythritol [Nikken Chemicals Co.,

Ltd. make:42-mesh (350 micrometers) path article] and ascorbic acid. After adding by the formula of the following table 13 of 11, respectively and mixing for 3 minutes, 240ml of water is used, and they are the spray pressure of 1.5kg/cm2, and spraying liquid speed 24 ml/min. Granulation was performed. Screening was carried out by 16 mesh sieves (1000 micrometers) after dryness, the crystalline cellulose was added by the formula of the following table 13 of 11, the magnesium stearate was added further 0.5weight %, and it mixed. Next, it tableted with the pestle of the 10mmphi round-corner planum using the single-engined tableting machine by the tablet weight of 400mg, and three kinds of tableting preassure power. The result examined about the obtained tablet is shown in 11 of the following table 14.

Work example 12 Ascorbic acid of the work example 11 was replaced with the thiamin mononitrate, and the same operation as a work example 11 was performed by the formula of Table 13 of 12. The result examined about the obtained tablet is shown in 12 of Table 14.

表１３　処　方

| 実　施　例 | | 11 | 12 |
|---|---|---|---|
| 成分 | エリスリトール | 240ｇ | 380ｇ |
| | アスコルビン酸 | 40ｇ | － |
| | 硝酸チアミン | － | 20ｇ |
| | 結晶セルロース | 120ｇ | 40ｇ |
| 合　計 | | 400ｇ | 440ｇ |

表１４　製剤特性

| 実　施　例 | | 11 | | | 12 | | |
|---|---|---|---|---|---|---|---|
| 打錠圧 | (kg／杵) | 361 | 546 | 1039 | 275 | 1125 | 1425 |
| | (kg／cm²) | 460 | 696 | 1324 | 350 | 1433 | 1815 |
| 硬度 | (kg) | 3.5 | 5.3 | 9.8 | 0.5 | 2.1 | 3.0 |
| 口腔内崩壊、溶解時間（秒） | | 25 | 31 | 43 | 16 | 22 | 20 |
| 崩壊時間（秒） | | 10 | 17 | 42 | 16 | 17 | 20 |
| 落下衝撃強度（%） | | 0 | 0 | 0 | 10 | 0 | 0 |
| 密度（mg／cm³） | | 1110 | 1221 | 1317 | 1113 | 1254 | 1286 |
| 備　考 | | キャッピングなし ザラツキ感なし | | | キャッピングなし ザラツキ感なし | | |

Work example 13 To a fluid bed granulation drier, they are erythritol [Nikken Chemicals Co., Ltd. make:42-mesh (350 micrometers) path article], cimetidine, a crystalline cellulose, and hydroxypropylcellulose. After adding by the formula of the following table 15, respectively and mixing for 3 minutes, 100ml of 8 w/v% solution of D-mannitol is used, and they are the spray pressure of 1.5kg/cm2, and spraying liquid speed 20 ml/min. Granulation was performed. Screening was carried out by 16 mesh sieves (1000 micrometers) after dryness, and the magnesium stearate was added 0.5weight % and it mixed. It tableted with the pestle of the 10mmphi round-corner planum using the single-engined tableting machine by the tablet weight of 400mg, and three kinds of tableting preassure power. It examined about the obtained tablet.

A result is shown in the following table 16.

表１５　処　方

| 実　施　例 | | 13 |
|---|---|---|
| 成分 | エリスリトール | 342ｇ |
| | シメチジン | 50ｇ |
| | 結晶セルロース | 20ｇ |
| | 低置換ヒドロキシプロピルセルロース | 20ｇ |
| | Ｄ－マンニトール | 8ｇ |
| 合　計 | | 440ｇ |

表１６　製剤特性

| 実施例 | | 13 | | |
|---|---|---|---|---|
| 打錠圧 | (kg／杵) | 275 | 595 | 1450 |
| | (kg／cm²) | 350 | 758 | 1847 |
| 硬度 | (kg) | 0.6 | 1.3 | 4.1 |
| 口腔内崩壊、溶解時間（秒） | | 31 | 30 | 38 |
| 崩壊時間（秒） | | 22 | 22 | 25 |
| 落下衝撃強度（%） | | 20 | 0 | 0 |
| 密度（mg／cm³） | | 1101 | 1205 | 1322 |
| 備考 | | キャッピングなし<br>ザラツキ感なし | | |

To a work-example 14(1) fluid-bed granulation drier, it is 5400g of cetraxate hydrochloride, After putting in Aspartame 81g and corn starch 275.4g and mixing for 3 minutes, granulation was performed by spray pressure 1.75kg/cm2 and spraying liquid speed 120 ml/min using 2520ml of 3 w/v% polyvinyl alcohol solution which dissolved scopolia extract 108g. After dryness, screening was carried out, the whole grain was carried out by 16 mesh sieves (1000 micrometers), and A granulation was obtained.

(2) To a fluid bed granulation drier, they are 3000g of precipitated calcium carbonate, 1500g of magnesium hydroxide, Erythritol 1050g, and corn starch 240g. After putting in and mixing for 3 minutes, granulation was performed by the spray pressure of 2.75kg/cm2, and spraying liquid speed 120 ml/min using 2000ml of 3 w/v% polyvinyl alcohol solution. After dryness, screening was carried out, the whole grain was carried out by 16 mesh sieves (1000 micrometers), and the B granule was obtained.

(3) Erythritol 5490g and corn starch 306g were put into the fluid bed granulation drier, and granulation was performed by the spray pressure of 1.5kg/cm2, and spraying liquid speed 120 ml/min using 540ml of 10 w/v% scopolia extract liquid, and 1700ml of purified water. After dryness, screening was carried out, the whole grain was carried out by 16 mesh sieves (1000 micrometers), and C granulation was obtained.

(4) After adding 6g of light anhydrous silicic acid, and corn starch 102g to 12g of l-menthol and mixing well, the mortar ground and l-menthol 10 trituration was obtained.

(5) Add 60g and 45g of magnesium stearate for l-menthol 10 trituration obtained above (4) by balance picking and this 1950g, respectively in C granulation obtained by 1170g and the above

(3) in the B granule obtained by 660g and the above (2) in A granulation obtained above (1). It mixed. Next, it tableted with the pestle of the 13mmphi average R using the single-engined tableting machine by the 1-dose weight of 647.5mg, and three kinds of tableting preassure power. The result examined about the obtained tablet is shown in Table 18.

表１７　　製剤処方

| 成　　分 | | 仕込み量（ｇ） |
|---|---|---|
| A顆粒 | 塩酸セトラキサート | 5400 |
| | ロートエキス | 108 |
| | アスパルテーム | 81 |
| | ポリビニルアルコール | 75.6 |
| | トウモロコシデンプン | 275.4 |
| | 小　　計 | 5940 |
| B顆粒 | 沈降炭酸カルシウム | 3000 |
| | 水酸化マグネシウム | 1500 |
| | ポリビニルアルコール | 60 |
| | エリスリトール | 1050 |
| | トウモロコシデンプン | 240 |
| | 小　　計 | 5850 |
| C顆粒 | ロートエキス | 54 |
| | エリスリトール | 5490 |
| | トウモロコシデンプン | 306 |
| | 小　　計 | 5850 |

表１８　　製剤特性

| 打錠圧 | | 硬　度 | 口中崩壊時間 | 崩壊時間 |
|---|---|---|---|---|
| (kg) | (kg／cm²) | (kg) | (秒) | (秒) |
| 841 | 634 | 4.3 | 64.9 | 32.8 |
| 1031 | 777 | 4.8 | 75.1 | 29.9 |
| 1328 | 1001 | 6.3 | 85.6 | 31.4 |

Work example 15 To a fluid bed granulation drier, they are erythritol [Nikken Chemicals Co., Ltd. make:42-mesh (350 micrometers) path article], corn starch, anhydrous caffeine, the thiamin mononitrate, a pyridoxine hydrochloride, calcium pantothenate, a nicotinamide, and Aspartame. After adding by the formula of the following table 19, respectively and mixing for 3 minutes, 100ml of 5 w/v% solution of a coffee extractant is used, and they are the spray pressure of 1.5kg/cm2, and spraying liquid speed 15 ml/min. Granulation was performed. After dryness, 16 mesh sieves (1000 micrometers)
Screening was come out and carried out, 1 weight % and the magnesium stearate were added 0.5weight %, and 10 trituration (what added the l-menthol 1 weight part and the light-anhydrous-silicic-acid 0.5 weight part to the corn starch 8.5 weight part, and carried out preferential grinding with the mortar) of l-menthol was mixed. Next, it tableted with the pestle of the 8mmphi round-corner planum using the single-engined tableting machine by the tablet weight of 240mg, and two kinds of tableting preassure power. The result examined about the obtained tablet is shown in the following table 20.

表１９

| 実　施　例 | | 15 |
|---|---|---|
| 成分 | エリスリトール | 176ｇ |
| | トウモロコシデンプン | 334ｇ |
| | 無水カフェイン | 50ｇ |
| | 硝酸チアミン | 3.3ｇ |
| | 塩酸ピリドキシン | 1.7ｇ |
| | パントテン酸カルシウム | 7ｇ |
| | ニコチン酸アミド | 5ｇ |
| | コーヒー抽出物 | 5ｇ |
| | アスパルテーム | 18ｇ |
| 合　計 | | 600ｇ |

表２０　製剤特性

| 実　施　例 | | 15 | |
|---|---|---|---|
| 打錠圧 | (kg／杵) | 618 | 1025 |
| | (kg／cm²) | 1230 | 2040 |
| 硬度　(kg) | | 0.5 | 2.0 |
| 口腔内崩壊、溶解時間（秒） | | 30 | 45 |
| 崩壊時間（秒） | | 40 | 67 |
| 落下衝撃強度（%） | | 40 | 0 |
| 密度（mg／cm³） | | 960 | 960 |

Industrial availability Since it has prompt disintegration and solubility and administration has strong hardness easily when it puts in in the oral cavity and into water, the rapidly disintegrable compression molding of this invention is excellent in the preservation stability in a manufacturing process or a distribution process.

Therefore, it can use conveniently for sick treatment and prevention of the patient applied according to the medicinal properties to contain especially an old man, a child, and the patient

for whom a deglutition is difficult.
Moreover, according to the manufacturing method of this invention, the rapidly disintegrable compression molding which has the above outstanding characteristics can be manufactured very easily, without requiring a complicated manufacturing process and special equipment. Furthermore, since the manufacturing method of this invention is the dry type tableting method, it is applicable also to combination drugs, such as a medicine which carries out an incompatibility to mutual [ lock / by a multi-granulation method / a tablet a lamination lock, etc. ].

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[Translation done.]